

CLAIMS

1. A nucleic acid molecule encoding human p53 which comprises:

at least one intragenic suppressor mutation, which is capable of suppressing a mutation of human p53 which occurs in human cancers when said intragenic suppressor and cancer mutations are present in a cis configuration; wherein said at least one intragenic suppressor mutation is selected from the group consisting of:

T81S; A83V; P87R; Q100L; Q100R; Q104P; F113L; L114V; T118M; V122I; C124S; K139R; Q144L; W146R; Q165L; V172I; H178Y; S183T; A189V; F212L; E224G; S227P; S227T; D228N; D228A; D228E; C229W; T230S; T231I; I232V; H233R; H233Y; Y234F; N235K; N235S; Y236N; N239M; N239W; N239L; N239F; N239R; N239H; S240Q; S240T; S240R; D281G; E285G; E285K; E294G; G325R; E343V; E346G; D352G; and combinations thereof.

2. A nucleic acid molecule encoding human p53 which comprises:

a set of at least one intragenic suppressor mutation, wherein said set is capable of suppressing a mutation of human p53 which occurs in human cancers when said intragenic suppressor and cancer mutations are present in a cis configuration; wherein said set is selected from the group consisting of:

F113L;
 L114V+T123P+V172I+A189V;
 T123P+A189V;
 S227P+N239Y;
 T118M+H168R;
 V122I+C124S+H168R;
 T123A+H168R;
 K139R+H168R+N239Y;
 H168R+T231I;
 T123A+S240R;
 H178Y+S240R;
 D281G+E285G+G325R+E343V;
 E285K+D352G;
 E285K+E294G+E346G;
 T81S+A83V+S240R;
 P87R+Q100L+Q104P+Q144L+S240R;

Q100R+W146R+S240R;
Q165L+F212L+S240R;
S183T+S240R;
E224G+S240R;
S240R;
D228A + N235K + N239M;
D228E + N235K + Y236N + N239L;
I232V + H233R + Y234F + N235K + N239L;
N235K + S240T;
Y234F + N239L;
N235K + N239R;
H233Y + N239Y;
N239F;
N239Y + S240Q;
H233Y + N235K + N239Y;
N235K + N239Y;
N235S + N239Y + S240N;
D228N + N239Y;
N235K + N239W;
D228E + N239Y;
N235K + S240N;
N239W;
T230S + N239Y;
S227T + N235K + N239Y;
H233R + N235S + N239R + S240R;
N239R;
N239R + S240R;
C229W + N239R + S240R;
N239L + S240R;
N239F + S240R;
I232V + N239H + S240R;
D228E + C229W + N235K + N239Y + S240R;
N239Y + S240R; and combinations thereof.

3. The nucleic acid of claim 1 further comprising a p53 mutation found in a cancer selected from the group consisting of: G245S; R249S; R273C; R273H; C141Y, V157F, R158L, Y163C, V173L, V173M, Y205C, Y220C, G245C, R249M, V272M, R273L, and E286K.
4. The nucleic acid of claim 1 further comprising at least one mutation of human p53 found in a cancer.
5. The nucleic acid of claim 2 further comprising a p53 mutation found in a cancer selected from the group consisting of: G245S; R249S; R273C; R273H; C141Y, V157F, R158L, Y163C, V173L, V173M, Y205C, Y220C, G245C, R249M, V272M, R273L, and E286K.
6. The nucleic acid of claim 2 further comprising at least one mutation of human p53 found in a cancer.
7. A human p53 protein which comprises:

at least one intragenic suppressor mutation which is capable of suppressing a mutation of human p53 which occurs in human cancers when said intragenic suppressor and said cancer mutations are present in a cis configuration; wherein said intragenic suppressor mutation is selected from the group consisting of:

T81S; A83V; P87R; Q100L; Q100R; Q104P; F113L; L114V; T118M; V122I; C124S; K139R; Q144L; W146R; Q165L; V172I; H178Y; S183T; A189V; F212L; E224G; S227P; S227T; D228N; D228A; D228E; C229W; T230S; T231I; I232V; H233R; H233Y; Y234F; N235K; N235S; Y236N; N239M; N239W; N239L; N239F; N239R; N239H; S240Q; S240T; S240R; D281G; E285G; E285K; E294G; G325R; E343V; E346G; D352G; and combinations thereof.
8. A human p53 protein which comprises:

a set comprising at least one intragenic suppressor mutation which is capable of suppressing a mutation of human p53 which occurs in human cancers when said intragenic suppressor and said cancer mutations are present in a cis configuration; wherein said set is selected from the group consisting of:

F113L;
 L114V+T123P+V172I+A189V;
 T123P+A189V;
 S227P+N239Y;
 N239Y;
 T118M+H168R;
 V122I+C124S+H168R;
 T123A+H168R;

K139R+H168R+N239Y;
H168R+T231I;
T123A+S240R;
H178Y+S240R;
D281G+E285G+G325R+E343V;
E285K+D352G;
E285K+E294G+E346G;
T81S+A83V+S240R;
P87R+Q100L+Q104P+Q144L+S240R;
Q100R+W146R+S240R;
Q165L+F212L+S240R;
S183T+S240R;
E224G+S240R;
S240R;
D228A + N235K + N239M;
D228E + N235K + Y236N + N239L;
I232V + H233R + Y234F + N235K + N239L;
N235K + S240T;
Y234F + N239L;
N235K + N239R;
H233Y + N239Y;
N239F;
N239Y + S240Q;
H233Y + N235K + N239Y;
N235K + N239Y;
N235S + N239Y + S240N;
D228N + N239Y;
N235K + N239W;
D228E + N239Y;
N235K + S240N;
N239W;
T230S + N239Y;
S227T + N235K + N239Y;
H233R + N235S + N239R + S240R;

N239R;
N239R + S240R;
C229W + N239R + S240R;
N239L + S240R;
N239F + S240R;
I232V + N239H + S240R;
D228E + C229W + N235K + N239Y + S240R;
N239Y + S240R; and combinations thereof.

9. The p53 protein of claim 7 further comprising a p53 mutation found in a cancer selected from the group consisting of: G245S; R249S; R273C; R273H; C141Y, V157F, R158L, Y163C, V173L, V173M, Y205C, Y220C, G245C, R249M, V272M, R273L, and E286K.
10. The p53 protein of claim 7 further comprising at least one mutation of human p53 found in a cancer.
11. The p53 protein of claim 8 further comprising a p53 mutation found in a cancer selected from the group consisting of: G245S; R249S; R273C; R273H; C141Y, V157F, R158L, Y163C, V173L, V173M, Y205C, Y220C, G245C, R249M, V272M, R273L, and E286K.
12. The p53 protein of claim 8 further comprising at least one mutation of human p53 found in a cancer.
13. A cell comprising the nucleic acid of claim 1.
14. A cell comprising the nucleic acid of claim 2.
15. A cell comprising the nucleic acid of claim 3.
16. A cell comprising the nucleic acid of claim 4.
17. A cell comprising the nucleic acid of claim 5.
18. A cell comprising the nucleic acid of claim 6.
19. A cell comprising the protein of claim 7.
20. A cell comprising the protein of claim 8.
21. A cell comprising the protein of claim 9.
22. A cell comprising the protein of claim 10.
23. A cell comprising the protein of claim 11.
24. A cell comprising the protein of claim 12.
25. A human p53 polypeptide which comprises:
a portion of human p53 protein, said portion comprising residues 94 to 292, and at least one intragenic suppressor mutation which is capable of suppressing a mutation of human p53 which occurs in human cancers when said intragenic suppressor and said cancer

mutations are present in a cis configuration; wherein said intragenic suppressor mutation is selected from the group consisting of:

T81S; A83V; P87R; Q100L; Q100R; Q104P; F113L; L114V; T118M; V122I; C124S; K139R; Q144L; W146R; Q165L; V172I; H178Y; S183T; A189V; F212L; E224G; S227P; S227T; D228N; D228A; D228E; C229W; T230S; T231I; I232V; H233R; H233Y; Y234F; N235K; N235S; Y236N; N239M; N239W; N239L; N239F; N239R; N239H; S240Q; S240T; S240R; D281G; E285G; E285K; E294G; G325R; E343V; E346G; D352G; and combinations thereof.

26. A human p53 polypeptide which comprises:

a portion of human p53 protein, said portion comprising residues 94 to 292, and a set of at least one intragenic suppressor mutation, wherein said set is capable of suppressing a mutation of human p53 which occurs in human cancers when said mutation is present in a cis configuration to the cancer mutation; wherein said set is selected from the group consisting of:

F113L;
L114V+T123P+V172I+A189V;
T123P+A189V;
S227P+N239Y;
N239Y;
T118M+H168R;
V122I+C124S+H168R;
T123A+H168R;
K139R+H168R+N239Y;
H168R+T231I;
T123A+S240R;
H178Y+S240R;
D281G+E285G+G325R+E343V;
E285K+D352G;
E285K+E294G+E346G;
T81S+A83V+S240R;
P87R+Q100L+Q104P+Q144L+S240R;
Q100R+W146R+S240R;
Q165L+F212L+S240R;
S183T+S240R;

E224G+S240R;
S240R;
D228A + N235K + N239M;
D228E + N235K + Y236N + N239L;
I232V + H233R + Y234F + N235K + N239L;
N235K + S240T;
Y234F + N239L;
N235K + N239R;
H233Y + N239Y;
N239F;
N239Y + S240Q;
H233Y + N235K + N239Y;
N235K + N239Y;
N235S + N239Y + S240N;
D228N + N239Y;
N235K + N239W;
D228E + N239Y;
N235K + S240N;
N239W;
T230S + N239Y;
S227T + N235K + N239Y;
H233R + N235S + N239R + S240R;
N239R;
N239R + S240R;
C229W + N239R + S240R;
N239L + S240R;
N239F + S240R;
I232V + N239H + S240R;
D228E + C229W + N235K + N239Y + S240R;
N239Y + S240R; and combinations thereof.

27. The p53 polypeptide of claim 25 further comprising a p53 mutation found in a cancer selected from the group consisting of: G245S; R249S; R273C; R273H; C141Y, V157F, R158L, Y163C, V173L, V173M, Y205C, Y220C, G245C, R249M, V272M, R273L, and E286K.

28. The p53 polypeptide of claim 25 further comprising at least one mutation of human p53 found in a cancer.
29. The p53 polypeptide of claim 26 further comprising a p53 mutation found in a cancer selected from the group consisting of: G245S; R249S; R273C; R273H; C141Y, V157F, R158L, Y163C, V173L, V173M, Y205C, Y220C, G245C, R249M, V272M, R273L, and E286K.
30. The p53 polypeptide of claim 26 further comprising at least one mutation of human p53 found in a cancer.
31. The p53 polypeptide of claim 25 which comprises residues 94 to 300.
32. The p53 polypeptide of claim 25 which comprises residues 94 to 312.
33. The p53 polypeptide of claim 25 which comprises residues 81 to 352.
34. The p53 polypeptide of claim 26 which comprises residues 94 to 300.
35. The p53 polypeptide of claim 26 which comprises residues 94 to 312.
36. The p53 polypeptide of claim 26 which comprises residues 81 to 352.